




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : C07C 69/003, 69/007, 69/02, 69/675, 69/608, 69/704, 69/74, 69/75, 69/757, 233/46, 305/08, 305/10, C07F 9/08, A61K 31/22, 31/23, 31/66, 31/20, 31/70, 31/72, A61P 31/12, 31/18, 31/22	A1	(11) International Publication Number: WO 00/37421 (43) International Publication Date: 29 June 2000 (29.06.00)
(21) International Application Number: PCT/AU99/01157 (22) International Filing Date: 21 December 1999 (21.12.99) (30) Priority Data: PP 7849 21 December 1998 (21.12.98) AU (71)(72) Applicant and Inventor: GHADIMINEJAD, Iraj [GB/AU]; 73 Tamboura Avenue, Baulkham Hills, NSW 2153 (AU). (74) Agent: F B RICE & CO; PO Box 668, Carlton South, 139 Rathdowne Street, Carlton, VIC 3053 (AU).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: NEPHRONIN: A SERIES OF COMPOUNDS FOR TREATMENT OF INFECTIOUS DISEASES AND CANCER <div style="text-align: center;"> $\begin{array}{c} \text{CH}_2\text{-(CH}_2)_l\text{-COO}^- \\ \\ \text{X-C-(CH}_2)_m\text{-COO}^- \\ \\ \text{CH}_2\text{-(CH}_2)_n\text{-COO}^- \end{array} \quad (I)$ </div> (57) Abstract <p>The present invention provides a non-proteinaceous compound isolatable from the urine of patients suffering from steroid responsive nephrotic syndrome. The compound has the following characterising features; (i) a molecular weight less than 1 KDa; (ii) binds specifically to heparin and heparan sulphate but not other glycosaminoglycans; and (iii) inhibits LPS induced production of TNF-α and/or IL-1α. The present invention also provides a compound of general formula: (I) in which l, m and n may be the same or different and integers of 0 to 10; and X is R-CO-O-, R-O-PO₂-O-, R-O-SO₂-O-, R-CO-NH-, R-CO-, R-O- or monosaccharide or oligosaccharide including amide substituted saccharides; in which R is a saturated, unsaturated, branched or cyclic carbon chain of up to 32 carbon atoms which optionally contains one or more hydroxyl groups, carbonyl groups, carboxylic acids groups, amino groups, phosphate groups or sulphate groups or combination thereof; and pharmaceutically acceptable salts and derivatives thereof.</p>		

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER		
Int Cl ⁷ : C07C 69/003, 69/007, 69/02, 69/675, 69/608, 69/704, 69/74, 69/75, 69/757, 233/46, 305/08, 305/10, C07F 9/08, A61K 31/22, 31/23, 31/66, 31/20, 31/70, 31/72, A61P 31/12, 31/18, 31/22		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols)		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) STN. Files CA. Registry. WPIDS. MEDLINE: keywords #urine, Nephrotic syndrome. MCN, SRN, FSGS, glomerular, HIV, septic, aids.		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Chemical Abstracts 129:335760, "Molecular complex and controlled-release of alpha-hydroxy acids", & WO 98/46217 A (Yu, Rucy J. et.al.) 22 October 1998. This disclosed compound RN 215172-81-9	2
X	Chemical Abstracts 126:108949, "Preparation of polymeric ocular inserts", & WO 96/39095 A (Domb A.J.) 12 December 1996. This disclosed compound RN 185951-09-1	2
X	Chemical Abstracts 125:67155, "A topical hair growth stimulant containing citric acid esters", & IN 173592 A (Hindustan Lever Ltd.) 11 June 1994. This disclosed compound RN 178435-26-2	2
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C <input checked="" type="checkbox"/> See patent family annex		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 8 February 2000		Date of mailing of the international search report 16 FEB 2000
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustalia.gov.au Facsimile No. (02) 6285 3929		Authorized officer  S.R. IDRUS Telephone No. (02) 6283 2536

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Chemical Abstracts 123:40705, "Cosmetic cleansing compositions containing hydroxy di- or tribasic acids or salts thereof", & WO 95/05154 A (Unilever Plc) 23 February 1995. This disclosed compound RN 162328-58-7	2
X	Chemical Abstracts 120:307465, "Hydroxamic acid-based bifunctional chelating compounds", & WO 94/05627 A (UAB Research Foundation) 17 March 1994. This disclosed compound RN 147219-28-1	2
X	Chemical Abstracts 118:87624, "Pharmaceutical transdermal formulations containing tricarboxylates", & JP 04202140 A (Sekisui Chemical Co. Ltd.) 22 July 1992. This disclosed compound RN 66558-76-7	2
X	Chemical Abstracts 115:256686, "Chemistry of micelles. 18. Cascade polymers:", & Newkome G. R. et.al., J.Org.Chem (1991) 56(25) 7162-7. This disclosed compound RN 136586-96-4	2
X	Chemical Abstracts 100:187878, "Citrate activation of NAD-specific isocitrate dehydrogenase from bovine heart", & Gabriel J.L., et.al, J.Biol.Chem.(1984), 259(3), 1622-8. This disclosed compound RN 89965-60-6	2
X	Chemical Abstracts 108:40124, "Citric acid ester emulsion polymerization emulsifiers", & DE 3605799 A (Bayer AG) 27 August 1987. This disclosed compound RN 112284-50-1	2
X	Chemical Abstracts 97:164032, "Thermal oxidation stabilizers", & JP 57073050 A (Murashino Chemical Research Institute) 7 May 1982. This disclosed compound RN 83348-55-4	2
X	Chemical Abstracts 94:194020, "Organic builders. XI. Building performances of malonate-type ether polycarboxylic acids", & Abe Yoshiro et.al., Yukagaku (1981) 30(1) 31-7. This disclosed compound RN 77319-18-7.	2
X	Chemical Abstracts 94:17408, "Organic builders X. Physicochemical properties of the aqueous solutions of ether polycarboxylate builders", & Abe Yoshiro et.al., Yukagaku (1980) 29(10), 748-54. This disclosed compound RN 76034-03-2	2
X	Chemical Abstracts 84:135271, "alpha, omega-diphenyl-alpha, omega-alkanediamines", & US 3929887 A (Endo Lab. Inc.) 30 December 1975. This disclosed compound RN 5617-46-9	2
X	Chemical Abstracts 82:88070, "Detergent mixture", & DE 2411479 A (Kao Soap Co.Ltd.) 19 September 1974. This disclosed compound RN 54262-054	2
X	Chemical Abstracts 66:37444, "Method of chelating with ether-group-containing sequestering agent", & US 3293176 A (White LeRoy Albert) 20 December 1966. This disclosed compound RN 14250-64-7	2
A	STN Medline On-line Abstract Accession No. 94077614, & Takahashi Y. et.al., PEDIATRIC RESEARCH (1993 Oct.) 34(4) 429-34.	1-13

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AUSTRALIAN PATENT OFFICE
SEARCH REPORT

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C (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	STN Medline On-line Abstract Accession No. 85012028. & Mimura K. et.al., METABOLISM: CLINICAL AND EXPERIMENTAL (1984 Oct) 33(10) 882-90.	1-13
A	STN Medline On-line Abstract Accession No. 84187246. & Martin R.S. et.al., JOURNAL OF LABORATORY AND CLINICAL MEDICINE (1984 May) 103(5) 798-810.	1-13

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 1-13
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

The scope of the claims directed to compounds is so broad that a complete search cannot be performed for economic reasons. The cited documents give just a small selection of compounds falling within the scope of claim 2: care has been taken to include compounds exemplifying each and every "R" possible under the definition provided.

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest
- ☐ No protest accompanied the payment of additional search fees.

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Information on patent family members

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report				Patent Family Member			
WO	98/46217	US	5877212	AU	68939/98		
WO	96/39095	AU	57757/96				
WO	95/05154	AU	76123/94				
WO	94/05627	US	5756825				
DE	3605799	EP	234416	US	4737543	JP	62199601
DE	2411479	JP	49116105	GB	1438066	NL	7403344

END OF ANNEX